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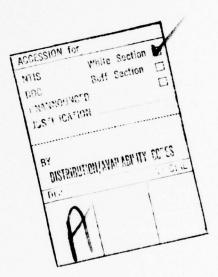
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have also been developed. Recent experimental work has focused on comparison of interfasicular graft repair with fasicular repair and end-to-end repair in a large group of primates using light histologic electron microscope, and electrical methods to evaluate results. During the past year, an implantable system for stimulating muscle in a long-term repetitive fashion has been designed and placed in a few animals and design of a radio-frequency triggering system is currently being worked on. In addition, our large clinical experience with nerve injuries has undergone computer storage and early analysis of some features, particularly the electrophysiologic ones, has been completed.



EVOKED POTENTIALS TO EVALUATE MECHANISMS OF PERIPHERAL NERVE REPAIR ANNUAL PROGRESS REPORT

July 1977

(for the period of 10 October 1976 to 30 September 1977)

by:

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ANNUAL REPORT ON:

17-6-C-6035

DAMD 76

Evoked Potentials to Evaluate Mechanisms of Peripheral Nerve Repair

Including Computerized, Non-Invasive Recording from Injured and/or

Regenerating Primate and Human Nerves. Study of Different Methods of

Repair Including Fascicular Suture and Interfascicular Autologous

Grafts As Well As Timing for Repair.

for 1977 - 1978 by:

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15 July 1977

LSU Medical Center 1542 Tulane Avenue New Orleans, LA 70112 Work accomplished during 1976-77 included completion of three series of primate experiments concerning interfascicular nerve repairs including grafts. This information was summarized in a manuscript, presented to the American Association of Neurological Surgeons in April, 1977, and was included in the pre-print manuscripts distributed at this meeting. Work is now underway to ready this information for more definitive publication and further studies concerning technique of nerve repair have been designed and are underway as will be described below and in the renewal request.

REPAIR EXPERIMENTS

Some time during the past year was spent designing and beginning two new repair protocols. Since epineurial repair when matched against fascicular repair fared somewhat better both electrically and histologically with eight of eleven animals having as their favored repair, an end-to-end epineurial one, it was decided to test the theory that preservation of and subsequent closure of the epineurium over the fascicular repair improves results. This then has been advocated by a number of surgeons including Smith, Millesi, French, and others. As in prior experiments, both tibial nerves of a healthy anesthetized primate were surgically exposed. Baseline evoked nerve action potential (NAP) and muscle action potential (EMG) as well as strain gauge studies of single twitch and tetanic contraction muscle tension were obtained. Both tibial nerves were severed at mid-thigh level and an end-to-end epineurial repair was done on one side using 8-0 nylon while on the other side fasicles of both the proximal and the distal stumps were dissected out in such a way as to spare the epineurium which was split longitudinally and then closed back over the 3 to 5 fasicles which had been sutured

with 8-0 nylon. Thus, each animal has an epineurial repair on one side to be compared with a fascicular repair plus epineurial closure on the opposite side. Six such animals have been lesioned and repaired to date, and four more are planned for lesioning and repair in the near future (see Renewal Request). It is planned at an interval of four, six, nine, or twelve months to re-operate on these limbs and re-record evoked NAP, EMG, and strain gauge studies of muscle tension. Nerves will be fixed in vivo and prepared for electron microscopic as well as light histologic study according to past protocols.

One of the observations made in the original repair series where interfascicular or fascicular repair was matched against epineurial repair was that the fascicular repair seemed to convert the more focal neuroma seen with an end-to-end epineurial repair into a lengthy neuroma spanning the segment of both the proximal and distal stumps where the fasicles had been dissected out. Histologically, it appeared that despite attempts to spare as much perineurium as possible around each fasicle that fasicles were losing axons to surrounding connective tissues and to other fasicles not only at the repair site but over the length of the dissection of the individual fasicle. Thus, it appears that theoretic exclusion of axonal crossover, which is a point cited favoring fascicular repair, was not a reality, at least within the limitations of the primate experiments described. As a result, with the help of Dr. Alan R. Hudson, an experiment was designed to answer this question more definitively. Both ulnar nerves of primates were exposed under anesthesia in the upper arm. Nerves were severed with glass and proximal stump and distal stump fasicles were dissected out under the microscope with an attempt to preserve as much of the perineurium around each fasicle as possible. End-to-end fascicular repair was then done as in prior experiments. However, in this experiment a 6-0 nylon loop was placed around both the proximal and distal stumps of one fasicle and not tied. The

intent of this experiment is to re-explore these fascicular repairs three months post-repair and to ligate the proximal stump with the nulon loop. After another 2 to 3 weeks have elapsed, the wounds will be re-explored and nerves removed for careful histologic studies with a especial attention to the distal stump fasicle marked with the untied nulon loop. If crossover occurs despite end-to-end fascicular repair then we would expect to see regenerating but otherwise healthy axons in the marked distal fasicle and degemerated axons in those distal fasicles not marked by a nulon loop. Five animals have been lesioned and repaired in this series, and it is planned to do three more so that sixteen nerves will be available for eventual study (see Renewal Request including protocol).

As outlined in the attachments which provide a copy of "Experimental Interfascicular Nerve Repair Including Grafts", three major experiments in the repair series have been completed. In the first series of experiments tibial nerves transected by glass after baseline electrical studies were repaired on one side by fasicle-to-fasicle or interfascicular repair while on the other side short interfascicular sural grafts were interposed between the proximal and distal stumps. Not only evoked nerve and muscle action potential but also muscle power measurements showed the end-toend fasicular repair to be ahead of the interfascicular graft repair in 10 of 16 animals. Nerves with interfascicular grafts showed the usual proximal and distal neuromas but in addition a large number of axons were seen escaping the fascicular structure over the course of the graft segment. Although not counted, axons in the fasicles distal to the graft segment seem to be less in number than comparable segments in the nerves repaired fasicle-to-fasicle. Although regeneration, as measured in this experiment, was slower in the grafted nerves than those repaired fasicle-to-fasicle, it should be stressed the nerves with grafts did nonetheless regenerate.

In the second group of experiments a segment of the tibial nerve 1 cm. in length was removed before repair. The animal's limbs were not immobilized, since prior experience with casting was unfavorable and we wished the animals to bear weight on their limbs and not be restrained in a chair. In addition, removal of a segment and subsequent suture produced a repair under tension. Pilot experiments in this group indicated that fascicular repair after segment resection would distract so epineurial end-to-end repair was matched with interfascicular graft repair. Even so, as can be seen in the summary table in the attachments, three of the end-to-end epineurial nerves distracted while only one of the nerves repaired by graft did so, thus emphasizing one of the recognized roles for grafts, that being the situation where tension on the repair site is great enough that likelihood of distraction is high. Nonetheless. epineurial end-to-end suture repair when distraction had not occurred was clearly ahead regeneratively by the parameters measured in these experiments. Histologically, regenerative patterns were similar to those described for Group I nerves. The epineurial end-to-end neuroma and its underlying axonal disorganization were more focal and confined to the suture site than was seen in those repaired end-to-end using a fascicular technique. As pointed out in the manuscript, despite increased tension on the non-graft or end-to-end epineurial repaired nerves, connective tissue proliferation was no greater than was seen in the grafted nerves and in the Group I repairs.

The third experimental group compared fasicle-to-fasicle or interfascicular repair with end-to-end epineurial repair. Eight of the 11 animals studied in this group had data favoring end-to-end epineurial repair. Striking again, when the fascicular repairs were viewed grossly as well as histologically was the fact that fascicular repair produced a less focal neuroma than seen with an end-to-end epineurial repair.

Neuroma extended over the length of the fascicular dissection necessary

to gain repair by the fasicle-to-fasicle technique. This occurred despite an attempt to preserve perineurium as much as possible around each fasicle. Histologically, the sections suggested that axons were escaping fasicles proximal to the actual repair site as well as at the repair site leading to neuroma both above and below the actual end-to-end fascicular repair. This theory, however, awaits further proof as outlined previously and as expanded in the renewal request.

Conclusions from the first three experimental groups include: (1) use of short, interfascicular autogenous grafts for transected nerve offers no apparent advantage when compared with end-to-end non-graft repair done either by a fascicular or epineurial technique; (2) tension on a repair within the limitations of these experiments does not appear to be an adverse factor providing distraction does not occur; (3) interfascicular or fasicle-to-fasicle repair does not offer an advantage over end-to-end repair although further experiments checking the efficacy of combining interfascicular repair with epineurial closure and studying the fate of axons in a given fasicle and whether or not they escape that fasicle need to be done; (4) despite the above, short interfascicular grafts do work and are capable of providing functional regeneration. Classic techniques to make up length such as transposition of the nerve, sacrifices on unimportant branches, mobilization of the proximal and distal stumps, and flexion of the extremity, remain useful and indicated for neural repair but when a gap is still present despite these techniques then relatively short interfascicular grafts can be used with some hope of functional recovery.

CLINICAL STUDIES

Clinical experience over a nineyear period with evoked nerve action potentials as well as other preoperative and intraoperative electrical studies as well as experience with transecting injuries was drawn

together in the early fall of 1976. In order to provide an adequate followup period the series of patients selected for this summary extended from June, 1966 until June, 1975, and thus there was at least a one-year followup on each patient. Sixty-five percent of the patients had three or more years of followup while 80% had two or more years followup, and the remainder had at least one year of followup. The series included 270 patients with 315 injured or lesion-involved elements. Excluded were cranial nerve injuries, superficial or sensory nerve injuries, and lower leg lesions. Some of the data concerning these patients is included in the attachments. In addition to reviewing the pertinent neurophysiologic information available concerning the behavior of injured and regenerating nerve the their proper selection of electrodiagnostic studies, conclusions in the chapter in press included: (1) indications for primary repair of lacerated nerves, particularly those lacerations involving proximal brachial plexus and sciatic complex; (2) one-third of lacerating injuries in our series still left the nerve with some degree of gross continuity; (3) the need for relatively acute management of aneurysms and fistulae associated with nerve injury, tight space syndromes due to fracture and contusion, foreign bodies lodged in or near nerve, blood clots under pressure, and selected pain problems and selected tumors was stressed; (4) personal experience with 255 injured neural elements in continuity due to gunshot wound, contusion, injury associated with fractures and stretch was reviewed. Importance of electrophysiologic testing as well as clinical evaluation was stressed since thorough electrical testing placed 65 injured neural elements into a different treatment category than would have been predicted from clinical examination alone. For example, in the group of 155 lesions in continuity felt to be complete on a clinical basis, intraoperative studies such as stimulation and nerve action potential recording showed that 30 were regenerating and these lesions fared well with only neurolysis rather than resection and suture. In addition, these patients quined functional results superior to what would have been predicted had their lesions been resected and a repair done. (See tables in the attachments). In the category of 100 lesions felt to be incomplete clinically 10 had no response to stimulation nor a nerve action potential, and resection and repair were necessary rather than neurolysis. Histologically, the resected specimens showed a degree of neurotmesis incompatible with successful functional regeneration. Presumably, these lesions were felt to be incomplete or recovering on clinical examination and/or electromyography, because of either shared innervational patterns or anomalous innervation; (5) providing the surgeon is prepared to both stimulate and record at the operating table exploration of lesions in continuity, 8 to 12 weeks post-injury seems to be optimal. This timing permits a physiologic decision whether to resect or to leave the lesion alone.

During the past year another 80 patients with nerve injuries were operated upon and had electrical recordings made both preoperatively and intraoperatively. These patients have been added to our computer system which now includes data on 412 patients. This data encompasses nerve or nerves injured, level of injury, injuring force, date of injury, results of preoperative electrical studies, results of intraoperative electrical studies, operation performed, histology of the lesion where available, and postoperative results along with the period of followup. Until recently, the system encompassed only those patients operated on who had an injury or tumor. In the last few months, we have begun to add to the system patients with spontaneous entrapment neuropathies and those who were evaluated clinically and electrically but not operated upon. During the past year a computer terminal has been obtained through this grant and one of our medical students has trained himself to utilize this to both place coded information into the system and to retrieve such information. An example of this is provided by the readouts

included in the attachments.

OTHER WORK

Operative recording studies continue. Several new electrode sets have been fabricated by the engineer who has also repaired instruments and helped Doctor Bratton fabricate a completely new apparatus for our strain gauge, muscle tension studies. The frame of the apparatus is made of plexiglass so it can be more readily kept clean than the older wood frame and metal unit. The brace to hold the tibial pin and to support the footplate as well as electrode carriers are of aluminum.

Work has also begun on a study of the effect of repetitive stimulation on deinnervated muscle. Instrumentation for this study has been a challenge since needed was a totally implantable and self-sustaining system for providing intermittent but accountable stimulation to gastrocnemius achilles musculature. Animals with tibial nerve lesions will be studied to see if repetitive muscle stimulation improves functional regeneration. Trials of various systems in pilot animals failed for a variety of reasons, but a workable system is now available and is described more fully in the grant renewal request. A microstimulator as well as a micropower pack have been developed by Doctor Happel and our engineer.

Work has been undertaken during this past year to ready another portable stimulating and recording apparatus for intraoperative recording for loan to Dr. Morton Spinner, a prominent New York hand surgeon so that two such instruments will be out on loan, one to the University of Toronto and the other to New York.

The peripheral nerve clinic which we have run in conjunction with orthopedic surgery and plastic surgery for a number of years has been moved to newly renovated quarters in the western wing of Charity Hospital on the first floor. This multi-disciplinary clinic continues to see three to six patients every other Friday and attempts to provide Charity

Hospital patients with a more comprehensive program of care for their peripheral nerve injuries or lesions.

It should be noted that during the past several years there has been a slight but definite increase in the number of nerve lesions in patients treated by a differential technique. Thus, partial or incomplete but focal lesions have had differential evaluation of the fasicles as suggested by Terzis, and according to their differential electrical evaluation as well as their appearance had neurolysis of some fasicle and repair of others. Internal neurolysis has also been utilized for a few lesions in continuity where pain of a non-causalgic nature has been a problem and yet there was useful axonal regeneration through the lesion. The patient's pain syndrome has been significant and has usually not been amendable or responsive to the usual medications nor blocks. Function has not been observed to improve immediately after such a procedure and is usually somewhat decreased, but relief of pain in some patients has made the procedure worthwhile.

COMPUTERIZED NERVE ACTION POTENTIAL OF RECORDING AND OTHER WORK

The investigators continue to study computerized non-invasive recording and each Tuesday afternoon is spent in this activity. As had been predicted, non-invasive recording is not as reliable as invasive recording of nerve action potentials since adjacent nerves may occassionally be either stimulated or recorded from and since both summation and amplification is necessary due to a decrement of the response from nerve to skin level. On the other hand, with experience, the procedure is not complicated, is non-invasive, and as a result is extremely well-tolerated by patients including infants. When NAP studies are used in conjunction with EMG a very accurate preoperative non-invasive picture of the lesion can be obtained. Special features include the rapid ability to do sensory NAP recording from distal median, ulnar, radial, peroneal, or

sural nerves. In brachial plexus lesions suspected to be at the root level one can both stimulate and record distal to the lesion. If an NAP is present and yet there is a complete motor and sensory deficit in the distribution of the nerve being tested then the lesion is at the level of the root between dorsal root ganglion and the cord for sensory fibers do not undergo regeneration and thus still conduct. This finding, of course, carries an extremely poor prognosis and suggests non-operative management. In the lower extremity, distal lower leg recordings can be of use for here distal tibial, peroneal, and sural (input from both tibial and peroneal) recordings indicate an index of more proximal function. However, more complete lesions at the buttocks and thigh level are difficult to evaluate in the early months following injury by this non-invasive technique even if they are regenerating. Distance between electrode sites and the dipole of the nerve is great and thus the decrement of any potential present dictates the need for high amplification and great summation which can produce misleading results. By the time sufficient axons have reqenerated distal to the knee and have reached more superficial and anatomically and sites, EMG, simple stimulation, or even clinical testing is accurate. On the other hand, we have been able to stimulate the femoral nerve of several patients with complete femoral palsies and recorded either quadriceps motor function, a femoral NAP, and/or an MAP, and thus the technique has sometimes been useful here.

Non-invasive computerized recording comes into its own with upper extremity lesions in continuity, particularly those around the elbow or in the forearm. Here there are both good distal sites for stimulation and proximal recording sites about or above the elbow.

PRESENTATIONS 1976-1977 RE: NERVE

- American Medical Association: "Emergency Management of Nerve Injury", Dallas, Texas; June 28, 1977.
- Pediatric Neurosurgery Course: "Nerve Injuries in Children", Atlanta, Georgia; September 19, 1977.
- 3) Surgical Biology Club II ACS: "Development of in-vivo Methods to Measure Regeneration of Nerve", Chicago; October 10, 1976.
- 4) Louisiana American College of Surgeons Chapter Meeting: "Nerve Lesion Management in Infants and Children:, November 14, 1976.
- 5) Congress of Neurologic Surgeons Meeting, October 25-29, 1976, New Orleans, Louisiana:
 - a) Restoration of facial function (Kline with Smith, J. and Brand, P.)
 - b) Important physiologic and clinical factors contributing to proper timing of nerve repair (Kline)
- 6) Medical College of South Carolina: "Modern Concepts of Management of Nerve Injuries", December 9, 1976.
- Cook County Postgraduate Course: "Nerve Injuries", Chicago, February 12, 1977.
- 8) Southern Neurosurgical Society: "Pediatric Nerve Injuries" (Bratton and Kline), Innisbrook, Florida, March 3, 1977.
- University of Oklahoma Medical School: Several nerve lectures, March 18-19, 1977.
- 10) American Association of Neurologic Surgeons Meeting, Toronto, April 24-28, 1977:
 - a) "Experimental Interfascicular Nerve Repairs Including Grafts" (Bratton, Hudson, & Kline)
 - b) "Newer Methods of Nerve Repair" (moderators: Hudson & Kline) (along with Millesi, Brooks, & Nulsen)
 - c) "Whether, When, and How to Operate on the Brachial Plexus" -Breakfast Seminar (Hudson & Kline) (along with Millesi, Brooks, &
 Whitcomb)

- 11) Northwestern Medical School: "Pediatric Nerve Injuries", May 7, 1977.
- 12) Eastern Virginia Medical School: Several talks on peripheral nerve injuries. Norfolk, Virginia, May 27, 1977.
- 13) Rocky Mountain Neurosurgical Society: "Preoperative Evaluation of a Patient with a Nerve Lesion" and "Postoperative Management of the Injured Peripheral Nerve"; Lake Tahoe, June 8-12, 1977.

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EXPERIMENTAL INTERFASICULAR NERVE REPAIRS INCLUDING GRAFTS*

Bert R. Bratton, M.D., Alan R. Hudson, F.R.C.S., and David G. Kline, M.D.

The use of autogenous interfasicular grafts to repair nerve injury requiring suture has been accepted by many who are actively involved in clinical peripheral nerve surgery. Millesi states that "nerve regeneration after grafting without tension is much better than after direct end-to-end suture under moderate tension even though the regenerating axons must cross two suture lines when grafts are used." A Nerve regeneration through a graft documented as far back as 1870 by Phillopeaux and Vulpian. Major contributions since then have been Huber, 1919; Balance and Duel, 1931; Davis, 1945; Seddon, 1965; and Marmor, 1972.

METHOD

Thirty-six adult rhesus monkeys had both tibial nerves transected at mid-thigh level and repaired. Sixteen monkeys (Group I) had an interfasicular autologous nerve graft repair in one limb and an interfasicular non-graft repair in the other limb. Thirteen monkeys (Group II) had a one centimeter segment of each tibial nerve resected followed by an interfasicular autologous nerve graft in one limb and an epineurial end-to-end repair in the other limb (non-graft interfasicular repair was impossible due to the degree of tension). Seven monkeys (Group III had the nerves lacerated with broken bottle glass followed by an interfasicular repair in one limb and an epineurial repair in the other limb. All thirty-six monkeys were allowed free movement post-operatively and no limb fixation was used.

Electrophysiologic data consisting of evoked nerve action potentials, evoked muscle action potentials, and muscle strength measurement of plantar flexion in response to single repetitive and tetanic stimuli of the tibial nerve were recorded pre-injury as a baseline and post-injury at 3, 6, 9, or 12 months. The operative microscope was used for all nerve repairs. 10-0 nylon was used for interfasicular repairs and 8-0 nylon for epineurial repairs.

All nerves were examined with the light and electron microscope.

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Group I

Evoked nerve action potentials could be recorded from all nerves upon re-exploration. Plantar flexion in response to tibial nerve stimulation could be recorded in each limb at re-exploration except the graft repaired nerve in one animal re-explored at 4 months. In four of the five animals re-explored at 4 months, muscle strength measurements were significantly better in the limb with the non-graft repaired nerve. The fifth animal at 4 months showed comparable return of function in both limbs. In three animals re-explored at 6 months, return of plantar flexion was significantly better in each non-graft repaired limb. Differences between graft and nongraft repaired nerves at 9 months were not as significant as at 4 and 6 months, but one animal with a flexion contracture on the non-graft side affected the average values. At 12 months, graft repair fared better in one, non-graft better in another while two were very comparable. Average values of return of muscle function (Table I) show limbs with non-graft repaired nerves clearly ahead of those with graft repair at 4 and 6 months while there was no significant difference at 9 and 12 months.

Histologically, the grafted nerves showed a typical neuroma at the proximal suture line. In the graft sections, well-defined segments with good fasicular arrangements were seen but a large number of regenerating axons were in extrafasicular loci. Disorganization of the distal suture line was quite similar to that seen at the proximal one. The non-graft interfasicular repair showed good fasicular pattern proximally, loss of fasicular pattern with neuroma formation at the suture line, and return of good fasicular pattern distally.

Group II

Due to tension on the repair site augmented by unrestricted motion, several distractions were noted upon re-exploration. Non-graft (epineurial) repair distractions were noted in one animal at 4 months, one at 6 months, and one at 12 months. There was also a graft repair distraction in one of

the nerves re-explored at 12 months.

Merve action potentials were recorded on all nerves except one animal re-explored at 9 months. Muscle function studies showed a consistent pattern. At 4 months three animals had a substantial difference in return of muscle function favoring the limb repaired by non-graft (epineurial) method. At 6 months two animals showed epineurial repaired nerves to be ahead in return of muscle function. At 9 months the values were close with non-graft repaired nerve favored in one animal and graft repaired nerve favored in the other. At twelve months only one of the three animals had continuity of both repairs and in this animal the epineurial repair was favored. Based on the averaged values of return of muscle function, the nongraft (epineurial) repaired nerves were significantly favored at 4 and 6 months. At 9 months, both repairs did equally as well and at 12 months, the non-graft repairs were slightly favored. Histologically, nerves had regenerative patterns similar to those described in Group I. Despite increased tension in the non-graft (epineurial repaired nerves), connective tissue proliferation was no greater than in Group I repairs.

Group III

Evoked nerve action potentials and plantar flexion in response to tibial stimulation were obtainable in all nerves re-explored. A partial distraction was noted in the interfasicular repaired nerve in one of the animals re-explored at nine months. The one animal re-explored at three months showed superior return of muscle function in the epineurial repaired limb. At six months both animals showed more return of muscle function in the epineurial repaired limb. At nine months the partially distracted interfasicular repair affected the results in one animal. The other animal showed quite comparable return of muscle function in both limbs. At twelve months both limbs with epineurial repairs fared better in terms of return of muscle function.

Averaged values of return of muscle function available at this writing (Table I), show the epineurial repaired nerves clearly ahead at all time intervals.

Intervals selected for restudy permitted axons to reach musculature and in this regard strain gauge measurement of muscle power was a more accurate measure of late functional nerve regeneration than either evoked nerve or evoked muscle action potentials. The superior return of muscle function seen in the non-graft nerves at both 4 and 6 months could be related either, in part, or entirely to differences in distance necessary for regenerating axons to reach distal inputs from the proximal stump. The addition of graft segments increased the distance for axons to travel by the length of the graft which was usually 1.0 to 1.5 cms. By 9 and 12 months, muscle function was increasingly comparable in both groups indicating that regenerative result in a repair with short grafts will eventually catch up to that achieved by end-to-end repair.

The addition of a second suture line necessary for a graft repair presents a theoretical second opportunity for loss of axons. Histologically, neither the interfasicular suture lines nor the grafted segments showed distinct fasicular patterns which should ideally be the theoretical advantage of an interfasicular repair. It was, therefore, not surprising that many of the regenerating axon clusters missed the graft segments in both groups and instead grew through extrafasicular tissue.

The fate of the extrafasicular axons within the graft segments presents an interesting problem. Explanation for the success of interfasicular grafts is probably related to the fact that, with the use of exceptionally short grafts, the extrafasicular axons are recaptured at the distal suture line and thus available to the distal stump.

The fact that the nerves repaired by an epineurial technique in Group

III fared better than those repaired by an interfasicular technique may again

be related to the loss of regenerating axons to extrafasicular tissue thus

making them unavailable for distal inputs. By closing the epineurium the

internal environment is re-established and potentially regenerating axons are

available to the distal stump and thus have at least some chance of reaching

more urstar end organs.

The concept proposed by dillest that tension of any sort on a repair is an adverse factor for regeneration was not supported by the quantitative electrophysiologic data or qualitative histologic studies in these experiments. Based on this data, use of short interfasicular autogenous grafts offers no advantage in functional nerve regeneration when compared with end-to-end non-graft sutures done either by interfasicular or epineurial techniques. Furthermore, data available to date, also suggests that interfasicular or fasicle to fasicle repair offers no advantage over end-to-end epineurial repair. Nonetheless, it is equally clear that short interfasicular grafts, when properly prepared and placed, do work. Despite extrafasicular loss of axons at each suture interface and delay in reaching end-inputs because of graft transit time, sufficient numbers of axons reach the distal nerve to produce some degree of functional reinnervation. Thus, after using the classical methods for making up length such as mobilization, transposition, sacrifice of tethering branches, and some flexion of the extremity, the remainder of the interstump gap, providing it is short, can be spanned by interfasicular grafts with some hope for successful reinnervation.

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GROUP I - SUMMARY Interfasicular Graft vs. Interfasicular Repair (Post-operative function expressed as averaged % of pre-laceration function)

	GR	AFT				NON-GRA	AFT	<u>F</u>	AVORED	REPAIR
MONTHS	NCV	RS	TC	N	CV	RS	TC	\underline{G}	NG	NEITHER
4	62.1	3.0	4.3	66	. 4	8.3	9.7	0	4	1
6	67.8	29.3	38.1	55	.5	42.1	51.2	0	3	0
9	65.3	53.5	48.8	60	.0	41.8	45.2	1	1	2
12	72.7	79.7	82.5	74	.7	79.8	81.3	1	2	1
								2	10	4

GROUP II - SUMMARY* Interfasicular Graft vs. Epineurial Repair Under Tension (Postoperative function expressed as averaged % of pre-laceration function)

	GR	AFT			NON-GR	AFT	<u>F</u>	AVOREL	REPAIR
MONTHS	NCV	RS	TC	NCV	RS	<u>TC</u>	<u>G</u>	NG	NEITHER
4	54.3	1.8	1.0	52.1	6.9	6.4	1	3	0
6	76.1	20.7	24.5	30.0	51.7	39.4	1	2	1
9	54.1	46.9	57.7	59.3	29.7	44.9	2	1	. 0
12	39.2	38.2	33.6	33.1	45.1	54.3	1	2	. 0
							5	8	1

^{*}Distraction of one non-graft studied at 4 months, one at 6 months, and one at 12 months as well as a graft distraction studied at 12 months affect the averaged data.

GROUP III - SUMMARY** Interfasicular Repair vs. Epineurial Repair (Postoperative function expressed as averaged % of pre-laceration function)

INT	ERFASI	CULAR		E	PINEUR	IAL	FA	VORED	REPAIR
MONTHS	NCV	RS	TC	NCV	RS	<u>TC</u>	<u>F</u>	E	NEITHER
3	66.7	3.6	0.8	64.6	4.2	8.8	0	1	2
6	89.0	40.2	45.2	75.4	65.5	58.2	0	4	0
9	57.5	44.6	35.8	73.8	53.5	77.6	0	1	1
12	79.9	63.7	72.9	76.4	79.5	82.6	0	2	0
							0	8	3

^{**}Four more animals have been lesioned and followed in this category but were not restudied in time for submission of this manuscript but will be included in the presentation.

KEY

NCV = Nerve Conduction Velocity
RS = Repetitive Stimuli
TC = Tetanic Contraction

Table la

Repair of Transections

		RESULTS	S		REOPERATION	TION
	No. of	Improved	Not Improved	No Followup	Neurolysis/	Neurolysis/Im'd Suture/Imp'd
Primary Repair	25	18	0,	1	3/2	3/2
Secondary Repair)		1	,	3	:
Grafts-	0,	4	ν.	0 1	0.	0 1
No Repair Possible	2	0	2	0	0	0
TOTALS	. 60	40	17	W	5/4	4/3

Table 1b

Interval Between Injury and Repair

TOTALS	Reoperation Neurolysis Re-suture	Secondary	Primary	
25	0	0	25	Immediate
4	0	۵.	0	0-1 mos
10	0	10	0	1-2 mos
14	1	12	0	2-4 mos
4	0		0	4-6 mos
U	2	. 1	0	6-9 mos
œ	2 2 0 3	2	0	9 mos or more

Table 2

Mechanism of Injury in Operated Lesions in Continuity (excludes transecting injuries)

	TOTAL	9	10	6	6			15		٣	3	2.5	3.1	37		20		2	6	5	255
	Other	0	0	0	0		0	0	0	0	0	1	1	2	2	0	0	0	0	1	2
Prior	014	0	1	0	0		0	0	0	0	0	0	1	2	0	0	0	0	0	0	4
Prior	ntn	0	0	0	0		1	0	0	0	. 0	1	4	9	0	0	0	0	0	0	12
	Ischemia	0	0	0	0		0	0	0	0	0	0	2	2	0	0	0	0	0	0	4
	Inj	0	0	0	0		0	0	0	0	0	3	1	0	7	4	4	0	1	0	14
	Tumor	0	, 1	1	1		1	1	0	0	0	3	2	3	0	2	2	2	1	0	20
	FX	0	1	1	1		3	3	3	0	1	9	1	2	0	0	0	0	2	0	24
	Stretch	E.	0	0	0		5	3	3	0	0	0	0	0	7	0	0	0	3 .	0	18
	Cont	e	~	2	2		1	1	1	1	0	5	7	2	0	2	2	0	0	0	3.1
•	USD	0	m	3	3		8	7	10	0	1	3	8	7	70	11	11	0	2	2	89
•	Lac	0	~	2	2		7	0	0	2	1	3	4	11	0	1	7	0	0	2	32
Lesion	Nerve	roots	trunks upper	middle	lower	cords		lateral	posterior	axillary	musculocutaneous	radial	median	ulnar	sciatic	tibi	ero	ibial	Perone	Femoral	ALS

Table 3

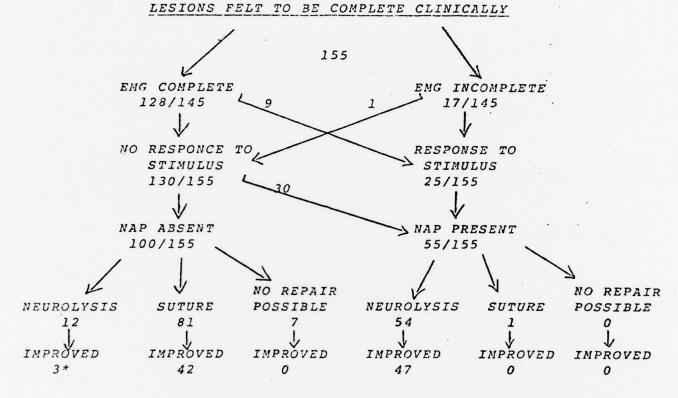
TO STATE OF THE PROPERTY OF TH

Interval Between Injury and Operation on Lesions in Continuity (in months) (excludes transections of nerve)

	0-1	1-2	2-3	3-4	4-5	5-6	6-9	9-12	over 12	TOTAL
roots	0	0	0	0	0	3	0	٣	0	9
trunks										
upper	0	7	2	2	0	0	7	8	1	10
middle	0	1	2	2	0	0	0	3	1	6
lower	0	1	2	2	0	0	0	3		6
cords										
medial	0	2	10	4	7	3	0	0	0	2.0
lateral	0	2	8	2	1	2	0	0	0	15
posterior	0	2	6	3	1_1	2	0	0	00	
axillary	0	0	1	1	0	1	0	0	0	3
musculocutaneous	0	0	1	1	0	0	0	0	1	3
radial	1	2	10	4	4	0	1	1	2	2.5
median	2	1		9	4	1	0	0	7.0	31
ulnar	3	9	12	4	2	2	2	2	9	37
sciatic	2	4	4	2	1	0	0	0	ī	14
tibial div.	2	9	2 .	3	1	2	0	1	3	20
peroneal div.	2	9	2	3	1	2	0	1	3	20
Tibial	0	0	0	0	0	0	0	0	2	2
Peroneal	3	0	0	2	0	2	I	0	1	6
Femoral	0	0	0	0	2	1	1	0	1	5
TOTAL	15	32	72	41	18	2.1	9	17	33	255

In 18 cases noted between 6 and 12 months or more, delay was necessitated by prior operation usually suture (14) usually in the median and ulnar categories.

TABLE 4



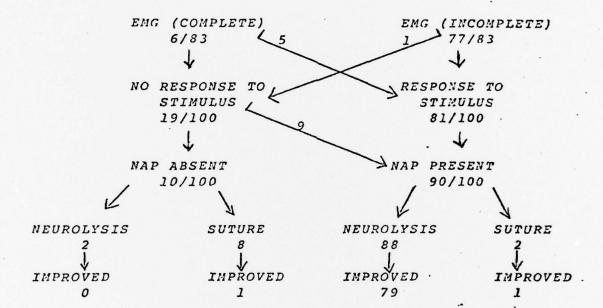
*2 of these 3 had an absent NAP while operated under tourniquet. An NAP might have been present if recording had been done after the tourniquet had been left down for a period.

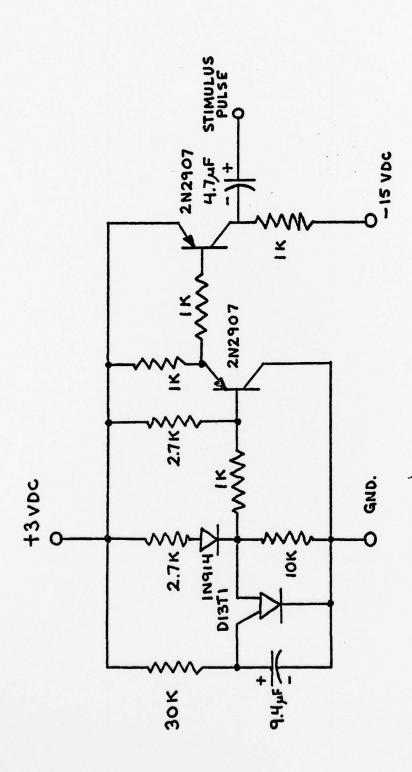
as of June, 1975

TABLE 5

LESIONS FELT TO BE INCOMPLETE CLINICALLY

100





STIMULATOR S-1

LOUISIANA STATE UNIVERSITY MEDICAL CENTER

Committee on Human Subjects at Risk

August 8, 1977

Dr. David G. Kline LSU Neurosurgery

Dear Kline:

In accordance with Committee procedures, we have reviewed on this date, August 8, 1977, the aspects of human subjects involved in your previously approved study entitled "Evoked Potentials to Evaluate Mechanisms of Peripheral Nerve Repair Including Computerized, Non-Invasive Recording"

In view of your report to the Committee that there have been no significant changes in procedure, or untoward reactions or problems concerned with your study, your present program complies with the requirements of the Committee concerning human subjects.

Very sincerely yours,

Francis C. Nance, M.D.

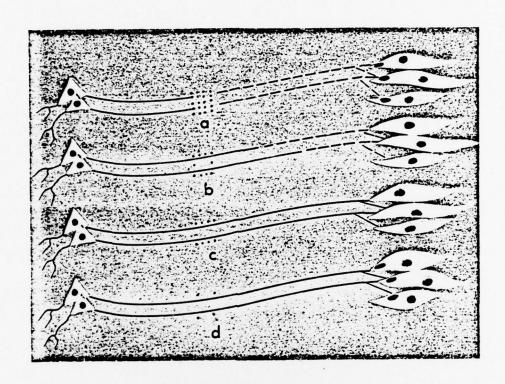
Chairman

FCN: 1dh

Consent Fo	orm for	Non-Invasive	Recording	of	Evoked	Nerve	Action	Potentials
				_				

The risks, complications, and possible benefits of non-invasive recording of evoked nerve action potentials have been explained to me in detail and I accept this procedure. Metal electrodes and electrode paste will be applied to the skin and stimulation of the estremity will be done using two of the electrodes. Response will be recorded by the other electrodes and processed by a number of electrical instruments including a computer and an oscilloscope. I understand that stimulation of the skin is mildly irritating but that this is done as part of routine electromyographic testing and that proper precautions to prevent electrical accidents have been taken just as with electromyography. I also understand that the test is experimental but may provide the physician with information which will improve the management of my case. In addition, I understand that at any time, I may withdraw my consent from the procedure and it will be terminated.

	Patient's Signature	
		*
Vitness)	(Witness)	



Schematic drawing of neurons (to the left), axons (middle), and an input site, motor end-plates and muscle (to the right). In a), an injury resulting in axonotemesis with secondary Wallerian degeneration has occurred. In addition to a relatively short area of retrograde axonal degeneration and demyelination, complete degeneration of axons and their coverings has occurred distally. In b) some weeks to months later axons have penetrated the injury and reached the distal stump but have not as yet obtained their distal inputs. In c), axons have reached muscle but an axon-to-end plate-to-muscle relationship is missing. In d), a more normal relationship has been re-established although axons are not as large in diameter nor as well myelinated as in uninjured nerve and conduction velocity is still slowed at this point. Electromyography may suggest reversal of deinnervation at c) while stimulation can predict useful regeneration at some point between c) and d). NAP recording may give information about relatively early regeneration occurring at b), or between b) and c).

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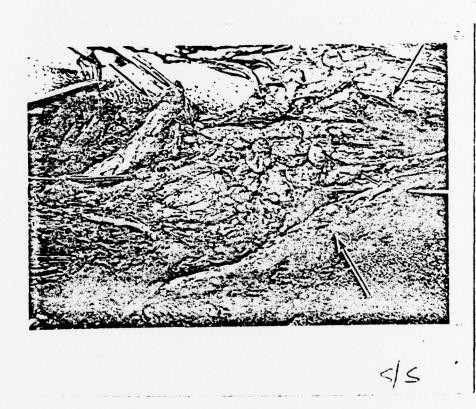
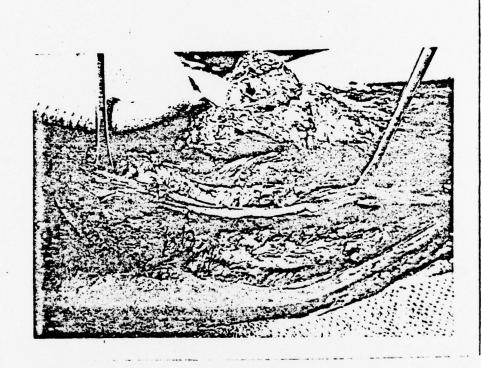
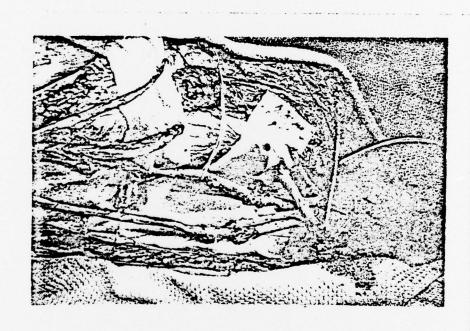


Figure 2 Transected median nerve (upper) and partially lacerated ulnar nerve (lower) at 3 months post-injury. At the time of repair of the brachial artery, the referring surgeon noted a cleanly severed median nerve and partially lacerated ulnar nerve but elected not to repair the median nerve. At exploration 3 months later a sizable gap between the stumps of the median nerve, as well as the neuroma in continuity of the ulnar nerve, was noted.



Despite mobilization, cable grafts were necessary for repair since the gap could not be closed after trimming both stumps back to healthy nerve tissue. One would wonder if this injury might not have fared better with primary repair. The partially lacerated ulnar nerve had an NAP of good amplitude conducting at 40 meters per second so only a neurolysis was done and then the nerve was transposed beneath pronator teres musculature. The patient has since gained an excellent result in the ulnar distribution but only pronator teres and forearm innervated flexor muscles have returned in the median distribution.

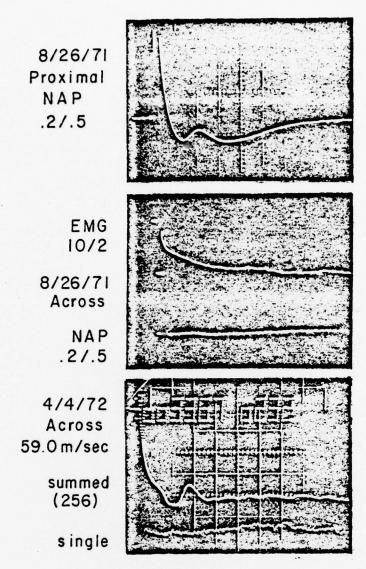
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Figure 4 Brachial plexus transected at axillary level by a radiator fan blade 10 weeks previously. Due to the relatively blunt nature of the original injury, secondary repair was elected but as shown in Figures 2 and 3, end-to-end repair could only be gained in a portion of this injury (the lower elements in the picture) while the remainder of the injury required interfasicular cable grafts from the sural nerves.

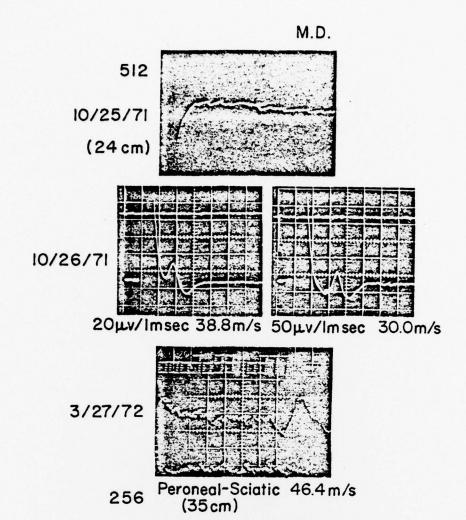
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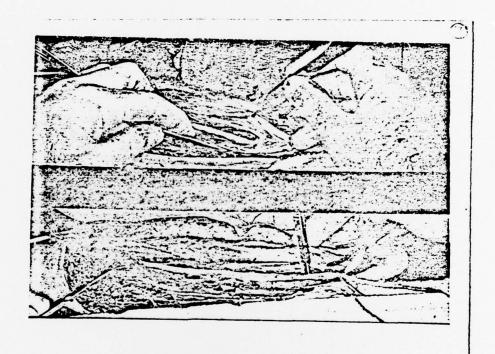
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Figure 5 Electrical tracings made from an ulnar nerve which had been primarily repaired after transection at the mid-forearm level 8 months before. Due to poor sensory as well as hypothenar muscle recovery, the nerve was re-explored. Upper inset shows an NAP recorded proximal to the suture neuroma. With electrodes placed across the neuroma as well as an EMG electrode placed in hypothenar musculature, neither an NAP nor an evoked muscle action potential could be recorded (middle inset). This necessitated resection and suture and histologic examination of the suture site and the distal stump of the nerve showed only fine, poorly organized and myelinated axons. Bottom inset shows a noninvasive computerized set of recordings made 7 months later. The bottom trace represents a single response while the top represents the summation of 256 individual traces and shows an adequate NAP indicating regeneration. Sensation in the ulnar distribution as well as hypothenar and some adductor pollicis muscle function has returned while interosseous and lumbricale function remains poor,

in press : Clinical Newsonwyer

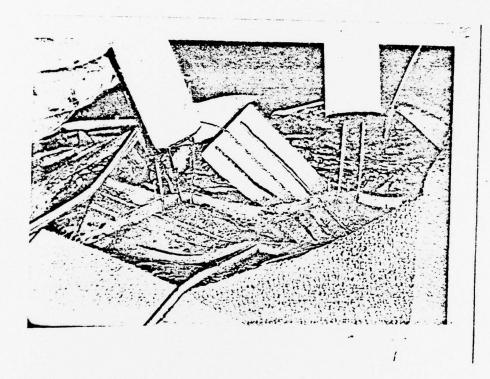


Non-invasive, computerized traces made preoperatively (upper inset) Figure 6 and postoperatively (lower inset) and operative, NAP's (middle inset). This patient sustained a qunshot wound to the proximal popliteal region resulting in a severe and almost complete sciatic palsy. Only a trace of plantar flexion was preserved. He was explored relatively early because the popliteal region felt tense and was discolored. On incising the intervening fascia between the hamstring masses and the fascia overlying the popliteal fossa, a clot extruded under some pressure. The missile had grazed the volar aspect of the sciatic nerve just proximal to its bifurcation into tibial and peroneal divisions and had partially lacerated a major branch of the popliteal artery accounting for the clot. After securing the injured popliteal branch, sciatic complex was split into tibial and peroneal divisions, and as can be seen by the middle inset an NAP could be recorded from both although conduction was slow and amplification necessary to record high. Over a 2-year period, the patient can now dorsiflex his foot not only against gravity but some pressure as well. Excellent plantar and toe flexion has returned. The lower trace shows both a single and summated sciatic potential obtained by stimulating the peroneal nerve over the head of the fibula by skin electrodes and recording from the proximal sciatic nerve below the buttock crease again by In press! Clinical skin electrodes.



Forearm musculature and median nerve in a young woman who accidentally Figure 7 injected Demerol into her brachial artery in the antecubital region nine months previously. This had been treated elsewhere by elevation of the limb and heparinization, but the patient developed a median, ulnar, and partial radial palsy in addition to Volkmann's contracture involving her forearm muscles. The upper inset shows musculature at the mid-forearm region replaced by fat and scar tissue while the scapel handle in the lower inset is pointing to a segment of the median nerve which was greatly narrowed due to her contracture. Since a small NAP could be recorded across this segment, the nerve was left alone and advancement of her forearm flexor musculature was carried out. She has had an acceptable recovery of function in the hand and forearm although she retains a great deal of disability. An immediate fasciotomy, exposure and treatment of the brachial artery, and probably neurolysis of her nerves was indicated in this case.

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Vinar nerve at mid-forearm level wounded by gunshot wound 3 months previously. Distal deficit was complete to both clinical testing and to electromyography, but a nerve action potential could be recorded across this lesion in continuity and as a result as much scar as possible was resected, the wound bed was debrided, and the nerve was covered with more healthy muscle. In the ensuing 12 months the patient made a partial but acceptable recovery of ulnar function. The proximal stump of this nerve had been exposed to permit the operator to record a more normal NAP at that site.

Recording electrodes (to the left of the picture) were moved across the neuroma confirming an NAP into the distal stump. Recording more distally (far to the left) showed no NAP at this point in time.

In press: Climical Newsterning

INFORMATION REQUESTED OF COMPUTER ON PERIPHERAL NERVE INJURIES

on 7-28-77

Excluding Entrapments in the Whole Series:

- A. (1) # of nerve injuries that were clinically complete (286) in which an operative NAP was present = 87
 - (2) # of nerve injuries that were clinically incomplete (184) in which operative NAP was absent = 24
- B. (1) # who had NAP (112) despite complete deinnervation by EMG = 16
 - (2) of these, those who also had response to stimulation = 6
 - (3) of these, those with neurolysis = 5, those with suture = 0, those with other = 1
- C. (1) # who did not have NAP (124) despite incomplete deinnervation by EMG = 16
 - (2) of these, those who had response to stimulation = 7
 - (3) of these, those with neurolysis = 6, those with suture = 0, those with other = 1
- D. (1) # who had pre-op NIR NAP but did not have operative NAP = 17
 - (2) # who did not have a pre-op NIR NAP but did have a operative NAP = 35; of these, those with response to stimulation = 12, those without response to stimulation = 20
- E. # nerves operated on since July, 1976 to July, 1977 = 95

For each of the above totals, there is a corresponding file which lists the patients with the respective traits. Contact Michael for further information.